Supplemental Materials

Title: Quantitative histogram analysis on intracranial atherosclerotic plaques: a pilot study using high resolution MRI

Authors: Zhang Shi, MD[1,2†]; Jing Li, MD[1†]; Ming Zhao, MD[3]; Wenjia Peng, MD[1*]; Zakaria Meddings, MEng[2]; Tao Jiang, MD[1]; Qi Liu, MD[1]; Zhongzhao Teng, PhD[2,4]; Jianping Lu, MD[1*]

Affiliations:

1. Department of Radiology, Changhai Hospital, Naval Medical University, Shanghai, China;
2. Department of Radiology, University of Cambridge, Cambridge, UK
3. Department of Neurology, Changhai Hospital, Naval Medical University, Shanghai, China;
4. Beijing Advanced Innovation Center for Biomedical Engineering, Beihang University, Beijing, China

[†] Equal contribution

[*]Corresponding authors

Study population

Inclusion criteria were: (1) suspected acute stroke or transient ischemic attack (TIA) (imaging within 1 month of the event onset); (2) with intracranial artery stenosis (≥30%); (3) at least one high-risk factor, including hypertension, diabetes mellitus, hypercholesterolemia, and cigarette smoking. Exclusion criteria were: (1) non-atherosclerotic intracranial arterial disease including vasculitis, Moya-Moya disease, dissection and reversible cerebral vasoconstriction syndrome; (2) suspected cardio-embolic stroke; (3) presence of significant stenosis of the extracranial carotid arteries (≥30%) assessed by ultrasound; (4) presence of ascending aortic arch atheroma as identified on MRI; (5) known coagulopathy; (6) heart or respiratory failure; (7) renal dysfunction (serum creatinine >133 μmol/L); (8) serious disturbance of consciousness; (9) intracranial hemorrhage; and (10) clinical contraindications to MRI, such as patients with pacemakers, certain types of metallic implants, and claustrophobia.

High resolution magnetic resonance imaging (hrMRI) acquisition

The GE system was equipped with an 8-channel phased-array head coil for middle cerebrovascular artery (MCA) imaging, and the Siemens system was equipped with a 20-channel phased array head and neck coil for basilar artery (BA) imaging. After an initial multi-plane localizer sequence, axial 3D time-of-flight (TOF) MR angiography was performed to identify the location of the MCA or BA stenosis. The hrMRI scanning parameters for MCA were: (1) 3D TOF MRA: TR/TE=29/3.4 ms, field of

view (FOV)=24×21 cm^2, slice thickness=1.2 mm, NEX=1, matrix=384×192, sequence duration=4.78 mins; (2) T2-weighted (T2W) FSE: TR/TE=2883/50 ms, FOV=10×10 cm^2, NEX=3, matrix=320×256, echo-train length (ETL)=20, slice thickness=2 mm, and sequence duration=3.85 mins; (3) T1-weighted (T1W) images: TR/TE=567/16 ms, FOV=10×10 cm^2, NEX=2, matrix=320×256, ETL=6, slice thickness=2 mm, and sequence duration=5 mins; (4) contrast enhancement T1-weighted (CE-T1W) images: a dose of 0.2 mmol/kg Gd-DTPA was injected by power injector at a rate of 2 ml/s followed by 15 ml of saline solution. Twelve slices were acquired for each of T1W, T2W and CE-T1W sequences with a spatial resolution of 0.31×0.39×2 mm^3. The scanning parameters for BA are similar to those used for MCA. The purposes of each sequence were: 1) 3D TOF MRA: MRA is particularly helpful to assess the arterial lumen condition. It is a routine and standard clinical protocol to identify narrowing. 2) DWI: This sequence is used to visualize white matter lesions and old and recent ischemia possibly associated with neuro symptoms. 3) hrMRI: hrMRI has been shown to provide a better visualization of atherosclerosis and subsequent stroke risk assessment.

Imaging analysis

The image quality was assessed with a method described previously[1]: each slice was graded on a 4-point scale (1=poor; 4=excellent) based on the overall signal-to-noise ratio and the contrast between the vessel wall and surrounding tissues. Images with grades $\geqslant$ 3 with most of lumen and outer wall boundaries visible were included in

this analysis and outer wall boundaries were manually segmented on T2W images at sites of maximum plaque area using CMRTools (Cardiovascular Imaging Solutions Ltd., UK). The stenosis ratio was measured independently on hrMRI images.[2, 3] The contrast enhancement ratio was measured at the slice of greatest enhancement normalized by the signal from adjacent gray matter (in a region of ~15 mm^2 at the cerebral cortex or hippocampus). Enhancement ratio=[signal of plaque (post-contrast)/signal of gray matter (post-contrast)]/[signal of plaque (pre-contrast)/signal of gray matter (pre-contrast)] × 100%. Minimal luminal area (MLA) was the lumen area at the most stenotic site. Plaque burden (PB) was defined as [1 – MLA/outer wall area] × 100%.[2, 3]

Reference

1. Lu M, Peng P, Cui Y, Qiao H, Li D, Cai J, et al. Association of progression of carotid artery wall volume and recurrent transient ischemic attack or stroke: A magnetic resonance imaging study. *Stroke*. 2018;49:614-620
2. Shi Z, Zhu C, Degnan AJ, Tian X, Li J, Chen L, et al. Identification of high-risk plaque features in intracranial atherosclerosis: Initial experience using a radiomic approach. *Eur Radiol*. 2018;28:3912-3921
3. Teng Z, Peng W, Zhan Q, Zhang X, Liu Q, Chen S, et al. An assessment on the incremental value of high-resolution magnetic resonance imaging to identify culprit plaques in atherosclerotic disease of the middle cerebral artery. *Eur Radiol*. 2016;26:2206-2214

Supplemental Table-I Comparison of AUC values between each feature

ROC	AUC	DA	sensitivity	specificity	PPV	NPV	LR-	LR+
MCA								
Stenosis	0.609	60.20	0.62	0.55	0.82	0.30	0.70	1.37
MLA	0.712	68.20	0.69	0.67	0.82	0.49	0.47	2.07
IPH	0.571	63.60	0.62	0.86	0.98	0.16	0.45	4.32
CV	0.8	73.90	0.75	0.72	0.82	0.62	0.35	2.67
Model of MCA	0.861	81.80	0.83	0.80	0.86	0.76	0.21	4.15
BA								
Stenosis	0.546	55.90	0.50	0.56	0.02	0.98	0.89	1.14
Enhancement	0.643	59.80	0.55	0.63	0.49	0.68	0.72	1.48
IPH	0.605	56.90	0.51	0.81	0.91	0.30	0.61	2.66
CV	0.708	64.70	0.61	0.67	0.56	0.72	0.58	1.86
Model of BA	0.804	79.50	0.79	0.77	0.67	0.86	0.27	3.37
All plaques								
Stenosis	0.563	55.80	0.56	0.56	0.59	0.52	0.79	1.26
Location	0.569	56.80	0.58	0.56	0.53	0.61	0.75	1.31
IPH	0.596	60.00	0.56	0.82	0.95	0.24	0.53	3.15
CV	0.766	70.00	0.69	0.72	0.75	0.65	0.44	2.43
Model of plaque	0.831	79.50	0.76	0.77	0.78	0.74	0.32	3.28

DA= Diagnosis accuracy

PPV= Positive predictive value; NPV= Negative predictive value

LR-= Negative likelihood ratio; LR+= Positive likelihood ratio

Supplemental Table-II The analysis of intra- and inter-observer reproducibility (intra-class coefficient)

	Intra-observer	Inter-observer
Enhancement ratio	0.893	0.918
Stenosis	0.891	0.913
PB	0.889	0.909
MLA	0.868	0.896
IPH	0.916	0.938
Area	0.918	0.921
Means	0.884	0.897
Standard deviation	0.968	0.989
Minimum value	0.917	0.928
Maximum value	0.926	0.949
Medians	0.859	0.889
Skewness	0.905	0.929
Kurtosis	0.921	0.965
CV	0.898	0.927